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**PALM INTRANET**

## Inventor Information for 10/272929

Inventor Name	City	State/Country
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WILLIAMS, MARTIN	CHARNY	CANADA

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 PALM INTRANET**Application Number Information**Application Number: **10/272929****Assignments**Filing or 371(c) Date: **10/18/2002**Effective Date: **10/18/2002**Application Received: **10/18/2002**Pat. Num./Pub. Num: **/20030118573**Issue Date: **00/00/0000**Date of Abandonment: **00/00/0000**Attorney Docket Number: **15493-1US**

PM/MG/al

Status: **41 /NON FINAL ACTION MAILED**Confirmation Number: **2858**Examiner Number: **77509 / WOITACH, JOSEPH**Group Art Unit: **1632** IFW IMAGE

Class/Subclass:

**514/044.000**Lost Case: **NO**

Waiting for Response

Interference Number:

Desc.

**Mail Non Final**Unmatched Petition: **NO**L&R Code: Secrecy Code:**1**Third Level Review: **NO**Secrecy Order: **NO**Status Date: **05/18/2006**Oral Hearing: **NO**Title of Invention: **MB-1 ANALOGS AND USES THEREOF**

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**PALM INTRANET****Inventor Name Search Result**

Your Search was:

Last Name = BEAUREGARD

First Name = MARC

Application#	Patent#	Status	Date Filed	Title	Inventor Name
<a href="#">09037948</a>	Not Issued	161	03/10/1998	GENETICALLY ENGINEERED RUMEN BACTERIAL STRAINS	BEAUREGARD, MARC
<a href="#">09810520</a>	6958992	150	03/16/2001	REGISTERING AN IP PHONE WITH AN IP PHONE SWITCH	BEAUREGARD, MARC
<a href="#">10272929</a>	Not Issued	41	10/18/2002	MB-1 analogs and uses thereof	BEAUREGARD, MARC
<a href="#">10625882</a>	Not Issued	71	07/24/2003	MB-1 analogs and uses thereof	BEAUREGARD, MARC
<a href="#">10776180</a>	Not Issued	71	02/12/2004	Method of mutagenic chain reaction	BEAUREGARD, MARC
<a href="#">11110069</a>	Not Issued	30	04/20/2005	Registering an IP phone with an IP phone switch	BEAUREGARD, MARC
<a href="#">11394281</a>	Not Issued	20	03/31/2006	System and method for scanning communications according to a policy	BEAUREGARD, MARC
<a href="#">60329759</a>	Not Issued	159	10/18/2001	MB-1 analogs and uses thereof	BEAUREGARD, MARC
<a href="#">60446518</a>	Not Issued	159	02/12/2003	Method of mutagenic chain reaction	BEAUREGARD, MARC
<a href="#">10306634</a>	Not Issued	61	11/27/2002	Expandable skin for safety restraint system	BEAUREGARD, MARC P.
<a href="#">60278909</a>	Not Issued	159	03/26/2001	Vehicle subfloor incorporating a ventilation system	BEAUREGARD, MARC P.

Inventor Search Completed: No Records to Display.

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1: [Khoudi H, Beauregard M.](#)

Related Articles, Links

The de novo designed nutritive protein MB-1Trp does not resist proteolytic degradation in alfalfa leaves.

Plant Physiol Biochem. 2005 Dec;43(12):1039-43. Epub 2005 Dec 13.

PMID: 16386425 [PubMed - indexed for MEDLINE]

2: [Carbonare CB, Carbonare SB, Carneiro-Sampaio MM.](#)

Related Articles, Links

Early acquisition of serum and saliva antibodies reactive to enteropathogenic Escherichia coli virulence-associated proteins by infants living in an endemic area.

Pediatr Allergy Immunol. 2003 Jun;14(3):222-8.

PMID: 12787303 [PubMed - indexed for MEDLINE]

3: [de Souza Campos Fernandes RC, Quintana Flores VM, Medina-Acosta E.](#)

Related Articles, Links

Prevalent transfer of human colostral IgA antibody activity for the enteropathogenic Escherichia coli bundle-forming pilus structural repeating subunit A in neonates.

Diagn Microbiol Infect Dis. 2002 Dec;44(4):331-6.

PMID: 12543537 [PubMed - indexed for MEDLINE]

4: [Xue HH, Kovanen PE, Pise-Masison CA, Berg M, Radovich MF, Brady JN, Leonard WJ.](#)

Related Articles, Links

IL-2 negatively regulates IL-7 receptor alpha chain expression in activated T lymphocytes.

Proc Natl Acad Sci U S A. 2002 Oct 15;99(21):13759-64. Epub 2002 Sep 27.

PMID: 12354940 [PubMed - indexed for MEDLINE]

5: [Moore SA, Kingston RL, Loomes KM, Hernell O, Blackberg L, Baker HM, Baker EN.](#)

Related Articles, Links

The structure of truncated recombinant human bile salt-stimulated lipase reveals bile salt-independent conformational flexibility at the active-site loop and provides insights into heparin binding.

J Mol Biol. 2001 Sep 21;312(3):511-23.

PMID: 11563913 [PubMed - indexed for MEDLINE]

6: [Campagna S, Cosette P, Molle G, Gaillard JL.](#)

Related Articles, Links

Evidence for membrane affinity of the C-terminal domain of bovine milk PP3 component.

Biochim Biophys Acta. 2001 Aug 6;1513(2):217-22.

PMID: 11470093 [PubMed - indexed for MEDLINE]

7: [Dopfer D, Nederbragt H, Almeida RA, Gaastra W.](#) Related Articles, Links  
 Studies about the mechanism of internalization by mammary epithelial cells of Escherichia coli isolated from persistent bovine mastitis. Vet Microbiol. 2001 Jun 6;80(3):285-96.  
PMID: 11337144 [PubMed - indexed for MEDLINE]

8: [Gagnon MC, Williams M, Doucet A, Beauregard M.](#) Related Articles, Links  
 Replacement of tyr62 by trp in the designer protein milk bundle-1 results in significant improvement of conformational stability. FEBS Lett. 2000 Nov 3;484(2):144-8.  
PMID: 11068049 [PubMed - indexed for MEDLINE]

9: [Alexander J, del Guercio MF, Maewal A, Qiao L, Fikes J, Chesnut RW, Paulson J, Bundle DR, DeFrees S, Sette A.](#) Related Articles, Links  
 Linear PADRE T helper epitope and carbohydrate B cell epitope conjugates induce specific high titer IgG antibody responses. J Immunol. 2000 Feb 1;164(3):1625-33.  
PMID: 10640784 [PubMed - indexed for MEDLINE]

10: [Grundy J, Morrison JJ, MacCallum JD, Wirtanen L, Beauregard M.](#) Related Articles, Links  
 Crystallization and stabilization of MB-1, a de novo designed protein for optimized feeding technology. J Biotechnol. 1998 Jul 30;63(1):9-15.  
PMID: 9764479 [PubMed - indexed for MEDLINE]

11: [Grundy JE, Wirtanen LY, Beauregard M.](#) Related Articles, Links  
 Addition of a poly-(6X) His tag to Milk Bundle-1 and purification using immobilized metal-affinity chromatography. Protein Expr Purif. 1998 Jun;13(1):61-6.  
PMID: 9631516 [PubMed - indexed for MEDLINE]

12: [Delneri MT, Carbonare SB, Silva ML, Palmeira P, Carneiro-Sampaio MM.](#) Related Articles, Links  
 Inhibition of enteropathogenic Escherichia coli adhesion to HEp-2 cells by colostrum and milk from mothers delivering low-birth-weight neonates. Eur J Pediatr. 1997 Jun;156(6):493-8.  
PMID: 9208250 [PubMed - indexed for MEDLINE]

13: [Damsky CH, Sheffield JB, Tuszynski GP, Warren L.](#) Related Articles, Links  
 Is there a role for actin in virus budding? J Cell Biol. 1977 Nov;75(2 Pt 1):593-605.  
PMID: 233748 [PubMed - indexed for MEDLINE]

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[0118] Design Strategy

[0119] The putative modifications to MB-1 structure are illustrated in FIG. 7.

The design strategy used here focused on two aspects: 1--the restrictive effect of a covalent bond between remote residues on the protein as a whole; and 2--the precise location of Cys which permits disulfide bridge formation. By choosing positions as far apart as possible, one can reduce the entropy gain upon unfolding for most of the protein. Thus, insertion of a bridge between helices I and IV would enclose a larger part of the polypolypeptide than a bridge involving other helices. Another consideration for using helix I is that this MB-1 segment of sequence is sensitive to proteolytic degradation. The restriction of helix I by Cys insertion could help prevent such a phenomenon.

[0120] The position of Cys in helices I and IV must allow sulphhydryl groups to be properly aligned in order to minimise strain induced by bridge formation.

On the basis of geometric models built for similar proteins, it appeared that position "d" of the heptad pattern used for MB-1 design would offer the best geometry for bridge formation. Therefore, L13 and M87 residues were selected for mutation to Cys. FIG. 7 depicts the expected location of the bridge in the mutant (hereafter referred to as MB-1LH, assuming it folds as per design).

Note that for proper alignment of position "d" in helices I and IV, a left-hand connectivity of the helices had to be assumed (i.e. the bundles are positioned such that when helix I is at the fore front, with its N-terminus pointing down, then helix II is placed to the left of helix I). A second scenario was considered, in which a right-hand connectivity could be specified. Examination

of the second model in FIG. 7 suggests mutations at positions "a" in helices I and IV, since positions "d" would be too far apart. By choosing M10

and L91 residues for mutation to Cys, we attempted to generate a mutant (named MB-1RH) that would resemble MB-1LH as much as possible, except for reversing its connectivity.

[0121] Disulfide bridges was also inserted into MB-1Trp. This protein is a derivative of MB-1 where Tyr62 was replaced by Trp. Position 62 in MB-1 was chosen for the emplacement of a spectroscopic probe at the moment of initial design. As shown on the model in FIG. 1, position 62 is part of the hydrophobic core, and a niche made of 5 Ala was built around it in order to accommodate a larger side chain in this region of the core. The replacement of Tyr by Trp was thought to improve on stability, and indeed, characterisation of MB-1Trp confirmed the strategy. MB-1Trp has a melting temperature of 55.degree. C. and is more resistant to protease action than MB-1. Here we are going to use MB-1Trp because of the increase in bulk offered by Trp in the core, in a way to compensate for the loss of volume consequent to the mutations used for bridge insertion.

## EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	2	"20040198681".pn.	US-PGPUB; USPAT; EPO; DERWENT	OR	OFF	2006/07/18 07:05
L2	2	"20040198681".pn. and MB	US-PGPUB; USPAT; EPO; DERWENT	OR	OFF	2006/07/18 07:14
L3	4	"20040198681".pn. or "20030118573".pn.	US-PGPUB; USPAT; EPO; DERWENT	OR	OFF	2006/07/18 07:26
L4	58237	MB- or (milk adj1 bundle)	US-PGPUB; USPAT; EPO; DERWENT	OR	OFF	2006/07/18 07:27
L5	58237	(MB- or mb) or (milk adj1.bundle)	US-PGPUB; USPAT; EPO; DERWENT	OR	OFF	2006/07/18 07:27
L6	410	(MB-1) or (milk adj1 bundle)	US-PGPUB; USPAT; EPO; DERWENT	OR	OFF	2006/07/18 07:27
L7	4	(milk adj1 bundle)	US-PGPUB; USPAT; EPO; DERWENT	OR	OFF	2006/07/18 07:28
L8	409	mb-1	US-PGPUB; USPAT; EPO; DERWENT	OR	OFF	2006/07/18 07:28
L9	32	mb-1 and milk	US-PGPUB; USPAT; EPO; DERWENT	OR	OFF	2006/07/18 07:28

## Woitach, Joseph

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**From:** Hensle, Kristine (ASRC)  
**Sent:** Monday, July 17, 2006 3:38 PM  
**To:** Woitach, Joseph  
**Subject:** The results have posted for SN 10/625882 seq ids 1 and an oligo search of 6, Search Acc.# 195497.

Dear Examiner Woitach,

I just checked SCORE and the results for your sequence search are there now. I would encourage you to use SCORE and see your results today.

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After downloading files, use Microsoft Word to view, manipulate and print.

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**Woitach, Joseph**

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**Sent:** Thursday, July 13, 2006 10:11 AM  
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**Subject:** sequence search request

Hello,

For application: 10/625,882,  
can you please do a search of SEQ ID NO: 1 (protein),  
and oligo search of SEQ ID NO: 6, the corresponding nucleic acid sequence.

Thank you,  
Joe

Joseph Woitach

(571) 272-0739

**Mailbox in Remsen 2C18**